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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/492,697	01/27/2000	Bernard Dujon	3495.0111-11	1254

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	23

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/492,697	DUJON ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-79* is/are pending in the application.

4a) Of the above claim(s) *38-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *45-47, 50-54, 57-61, 63, 65-69, 71-72, 74-79* is/are rejected.

7)☐ Claim(s) *48,49,55,56,62,64,70 and 73* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 09/27/02 has been acknowledged.

Claims 61-74 are newly filed claims.

Claims 38-74 are pending.

This application contains claims 38-44 drawn to an invention nonelected with traverse in Paper No. 13. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

► *If the claims are amended, added and/or canceled in response to this office action the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (http://www.uspto.gov) and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED.*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 45-47, 50-54, 57-61, 67, 71-72 and 74-79 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons of record as set forth in the office action mailed on 05/31/02.

The applicant argues that applicant has described many species that fall within the Group I intron encoded endonuclease sites. The applicant argues that fig-6 in the specification teaches the nucleotide sequences of recognition sites for the claimed species. The applicant further argues that office has provided no reasons why applicants species of endonucelase sites (as claimed) are not representative of all Groups I intron endonuclease sites (response, page 5). The applicant argues that the applicant teaches Class I-V of Group I intron encoded endonuclease sites and representative members of each group (response, page 6, para.1). The applicant argues that Belfort (exhibit-1) is objective evidence that applicant's specification discloses representative species of intron-encoded endonucleases. The applicant further argues that Turmel (exhibit-2) is objective evidence that I-TevII is an intron encoded endonucleases. The applicant argues that newly filed claims recite specific Group I intron encoded endonucleases sites.

However, this is not found persuasive because the scope of the instant invention as claimed encompasses any and all Group-I-intron-encoded endonuclease sites. At best the specification only discloses endonucleases sites for Class I (I-SceI, I-SceII, I-SceIII, I-SceIV, I-CsmI, I-PanI, I-CeuI, I-CreI) endocunclease sites that result in a 4 bp staggered cut with 3'OH overhang. The specification further discloses a Class II (I-TevI) endonuclease site that results in a 2 bp staggered cut with 3'OH overhang. However, the specification even fails to disclose the recognition sites nucleotide sequences and cleavage sites for and Class III (I-PpoI), Class IV (I-TevII) and Class V (I-TevIII) endonucleases (spec. page 27 and fig-6). In addition, the specification teaches that that Class III, IV and V endonuclease sites are not represented by any typical structural motifs (spec. page 27, lines 13-21). Similarly, Turmel et al teaches that I-Tev-

II leave 2nt 3'OH overhang but fails to disclose any motif specific to the class it represent (see Turmel page 2610, col2. para.1). In addition, the specification fails to disclose any consensus nucleotide sequences and/or structural motifs that represent a particular Class of Group-I encoded endonuclease sites that exist in nature. For example, the endonucleases of Class I (I-SceI, I-SceII, I-SceIII, I-SceIV, I-CsmI, I-PanI, I-CeuI, I-CreI) are structurally and functionally distinct endonucleases which cut structurally unique endonuclease sites. The art at the time of filing teaches that Group-I introns form a structural and functional groups of introns with wide spread irregular distribution among very diverse organisms and genetic systems (Dujon Gene 82:91-114, 1989, see abstract). The general knowledge in the art concerning Group I Intron encoded endonuclease does not provide any indication as how the structure of one Class of endonucelases site is representative of other Classes having concordant or discordant functions and/or restriction sites (Dujon Gene 82:115,-118 1989. see page 17, table-I). Besides Class I I-endonuclease sites (I-SceI, I-SceII, I-SceIII, I-SceIV, I-CsmI, I-PanI, I-CeuI, I-CreI) the specification fails to disclose the recognition nucleotide sequences and cleavage sites for a representative number of species belonging to Class II I-endonuclease sites, Class III I-endonuclease sites, Class IV I-endonuclease sites and Class V I-endonuclease sites.

The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d*

1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406).* In the instant case, Group I intron encoded endonucleases has been defined only by a statement of an endonucleases activity for each class, which conveyed no distinguishing information about the identity of whole genus, such as its relevant structural or physical characteristics. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only few members of this genus is not representative of the variants of genus and is insufficient to support the claim.

45-79

Claims 45-47, 50-54, 57-61, 63, 65-69, 71-72, 74-79 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant mammalian chromosome comprising an endonuclease site selected from I-SceI, I-SceII, I-SceIII, I-SceIV, I-CsmI, I-PanI, I-CeuI, I-CreI and I-TevI sites, does not reasonably provide enablement for any and all endonucleases sites selected from any and all Classes of Group-I intron encoded endonucleases sites. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention

commensurate in scope with these claims, for the same reasons of record as set forth in the office action mailed on 05/31/02.

The applicant argues that applicants are not required to disclose every species encompassed by their claims. The applicant argues that the newly filed claims 61-79 recites specific Group I intron encoded endonucleases as shown in figure-6 of the specification (response, pages 8-9).

However, this is not found persuasive because the scope of instant invention as claimed encompasses any and all endonucleases sites selected from any Class of Group I intron encoded endonuclease sites. At best the specification only discloses endonucleases sites for Class I (I-SceI, I-SceII, I-SceIII, I-SceIV, I-CsmI, I-PanI, I-CeuI, I-CreI) and Class II (I-TevI). The specification even fails to disclose the recognition sites nucleotide sequences and cleavage sites for and Class III (I-PpoI), Class IV (I-TevII) and Class V (I-TevIII) endonucleases (spec. page 27 and fig-6). In addition, the specification clearly teaches that that Class III, IV and V endonuclease sites are not represented by any typical structural motifs (spec. page 27, lines 13-21). Therefore, considering the guidance provided in the specification it is unclear how one skill in the art would use invention as claimed without the knowledge of a recognition and a cleavage site specific for a particular Group-I intron encoded endonuclease. The endonucleases sites of I-SceI, I-SceII, I-SceIII, I-SceIV, I-CsmI, I-PanI, I-CeuI, I-CreI) are structurally and functionally distinct sites that does not represent a consensus recognition sequence and cleavage sites for all classes of Group I endonuclease sites (see fig-6). Furthermore, the art at the time of filing teaches that Group-I introns form a structural and functional groups of introns with wide spread irregular distribution among very diverse organisms and genetic systems (Dujon Gene 82:91-114, 1989,

see abstract). The general knowledge in the art concerning Group I Intron encoded endonuclease does not provide any indication as how the structure of one Class of endonucelases site is representative of other classes having concordant or discordant functions (Dujon Gene 82:115,-118 1989. see page 17, table-I). Thus, in view of lack of specific guidance in the specification, the skilled artesian at the time of filing would be unable to use the claimed invention, without an excessive and undue amount of experimentation.

In addition, the scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970). The courts have clearly stated that a specification need not to disclose what is well known in the art. See, e.g., Hybritech Inc. V. Monoclonal Antibodies, Inc., 802 F. 2d 1367, 1385, 231 USPQ 81, 94(Fed. Cir. 1986). However, that general off-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific material or of any of the conditions under which a process can be carried out, undue experimentation is required: there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. *It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".* Genentech Inc. V. Novo Nordisk A/s, 42 USPQ2d 1005 (CAFC 1997). Furthermore, the instant specification does not comply with 35 U.S.C. 112 since nebulous expression of Group I endonuclease recognition sites do not contain a sufficiently explicit indication of usefulness of compounds and how to use them. The utility requirements must be met at the time of filing and

not after someone else identify a utility that had not been disclosed in the specification. The disclosure is insufficient where experimentation is necessary to determine actual uses, or possible lack of uses, of compounds, as well as how to employ them in a useful manner. For example, it cannot be presumed that a steroid chemical compound is "useful" under 35 U.S.C. 101, or that one skilled in the art will know "how to use" it, simply because compound is closely related only in a structural sense to other steroid compounds known to be useful (In re Kirk and Petrow, 153 USPQ 48 (CCPA 1967)). In instant case without sufficient guidance, identification of any and all Group-I endonucelase sites is not considered routine and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Claim Objections

Claims 48-49, 55-56, 62, 64, 70 and 73 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten independent form including all of the limitation of the base claim and any intervening claims.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-8724 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

S. Kaushal
Patent examiner

JEFFREY FREDMA
PRIMARY EXAMI